

PATENT COOPERATION TREATY

PCT

NOTIFICATION CONCERNING
SUBMISSION OR TRANSMITTAL
OF PRIORITY DOCUMENT

(PCT Administrative Instructions, Section 411)

From the INTERNATIONAL BUREAU

To:

BENT, Stephen, A.
Foley & Lardner
Suite 500
3000 K Street, N.W.
Washington, DC 20007-5109
ETATS-UNIS D'AMERIQUE

Date of mailing (day/month/year) 09 January 2001 (09.01.01)	IMPORTANT NOTIFICATION
Applicant's or agent's file reference 037147/0104	
International application No. PCT/US00/26113	
International publication date (day/month/year) Not yet published	
Applicant COHEN, Jonathan	International filing date (day/month/year) 22 September 2000 (22.09.00) Priority date (day/month/year) 24 September 1999 (24.09.99)

- The applicant is hereby notified of the date of receipt (except where the letters "NR" appear in the right-hand column) by the International Bureau of the priority document(s) relating to the earlier application(s) indicated below. Unless otherwise indicated by an asterisk appearing next to a date of receipt, or by the letters "NR" in the right-hand column, the priority document concerned was submitted or transmitted to the International Bureau in compliance with Rule 17.1(a) or (b).
- This updates and replaces any previously issued notification concerning submission or transmittal of priority documents.
- An asterisk(*) appearing next to a date of receipt, in the right-hand column, denotes a priority document submitted or transmitted to the International Bureau but not in compliance with Rule 17.1(a) or (b). In such a case, the attention of the applicant is directed to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.
- The letters "NR" appearing in the right-hand column denote a priority document which was not received by the International Bureau or which the applicant did not request the receiving Office to prepare and transmit to the International Bureau, as provided by Rule 17.1(a) or (b), respectively. In such a case, the attention of the applicant is directed to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.

<u>Priority date</u>	<u>Priority application No.</u>	<u>Country or regional Office or PCT receiving Office</u>	<u>Date of receipt of priority document</u>
24 Sept 1999 (24.09.99)	60/155,665	US	21 Dec 2000 (21.12.00)

REVIEWED BY

INITIALS JME DATE 12/3/07

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No. (41-22) 740 14 35

Authorized officer

Magda BOUACHA

Telephone No. (41-22) 338 83 38

Form PCT/B/304 (July 1998)

003759656

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From the INTERNATIONAL BUREAU

NOTICE INFORMING THE APPLICANT OF THE
COMMUNICATION OF THE INTERNATIONAL
APPLICATION TO THE DESIGNATED OFFICES

(PCT Rule 47.1(c), first sentence)

To:

BENT, Stephen, A.
Foley & Lardner
Suite 500
3000 K Street, N.W.
Washington, DC 20007-5109
ETATS-UNIS D'AMERIQUE

Date of mailing (day/month/year) 29 March 2001 (29.03.01)		
Applicant's or agent's file reference 037147/0104		IMPORTANT NOTICE
International application No. PCT/US00/26113	International filing date (day/month/year) 22 September 2000 (22.09.00)	
Applicant COHEN, Jonathan		

1. Notice is hereby given that the International Bureau has communicated, as provided in Article 20, the international application to the following designated Offices on the date indicated above as the date of mailing of this Notice:

US

In accordance with Rule 47.1(c), third sentence, those Offices will accept the present Notice as conclusive evidence that the communication of the international application has duly taken place on the date of mailing indicated above and no copy of the international application is required to be furnished by the applicant to the designated Office(s).

2. The following designated Offices have waived the requirement for such a communication at this time:

EP,JP

The communication will be made to those Offices only upon their request. Furthermore, those Offices do not require the applicant to furnish a copy of the international application (Rule 49.1(a-bis)).

3. Enclosed with this Notice is a copy of the international application as published by the International Bureau on 29 March 2001 (29.03.01) under No. WO 01/22086

REMINDER REGARDING CHAPTER II (Article 31(2)(a) and Rule 54.2)

If the applicant wishes to postpone entry into the national phase until 30 months (or later in some Offices) from the priority date, a demand for international preliminary examination must be filed with the competent International Preliminary Examining Authority before the expiration of 19 months from the priority date.

It is the applicant's sole responsibility to monitor the 19-month time limit.

Note that only an applicant who is a national or resident of a PCT Contracting State which is bound by Chapter II has the right to file a demand for international preliminary examination.

REMINDER REGARDING ENTRY INTO THE NATIONAL PHASE (Article 22 or 39(1))

If the applicant wishes to proceed with the international application in the national phase, he must, within 20 months or 30 months, or later in some Offices, perform the acts referred to therein before each designated or elected Office.

For further important information on the time limits and acts to be performed for entering the national phase, see the Annex to Form PCT/IB/301 (Notification of Receipt of Record Copy) and Volume II of the PCT Applicant's Guide.

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No. (41-22) 740 14 35

Authorized officer

J. Zahra

Telephone No. (41-22) 338 83 38

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(19) World Intellectual Property Organization
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- (21) International Application Number: PCT/US00/26113
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- (71) Applicant and
(72) Inventor: COHEN, Jonathan [US/US]; 10405 Broadfield CT., Potomac, MD 20854 (US).
- (74) Agents: BENT, Stephen, A. et al.; Foley & Lardner, Suite 500, 3000 K Street, N.W., Washington, DC 20007-5109 (US).
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- Published:
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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: A HIGH-THROUGHPUT SYSTEM FOR EVALUATING THE CLINICAL UTILITY OF MOLECULAR TARGETS IN TISSUE SAMPLES

(57) Abstract: An approach to establishing the clinical utility of a molecular target entails bringing a large quantity of different tissue samples into contact, in a high-throughput manner, with a stain that specifically binds a target molecule *in situ*, and then determining the extend to which the stain has bound the target molecule in the tissue samples. To this end, apparatus can be employed that comprises (i) a tissue microarray, having hundreds of small tissue samples upon which reagents may be applied; (ii) an automated staining instrument for applying reagents to the tissue samples and then carrying out most of the steps required for *in situ* hybridization and immunohistochemistry, and (iii) an imaging instrument to allow a user readily to ascertain the presence and/or the quantity of target in each of the samples.

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US00/26113

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : G01N 33/53, 33/567, 33/574; C12M 1/36, 1/38, 3/00

US CL : 435/7.2, 7.23, 288.3

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 435/7.2, 7.23, 288.3

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
STN, EAST

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y, P	US 6,103,518 A (LEIGHTON) 15 August 2000 (15/08/00), see especially column 1, line 9 to column 2, line 29.	1-20
X	KONONEN et al. Tissue microarrays for high-throughput molecular profiling of tumor specimens. Nature Med. July 1998, Vol. 4, No. 7, pages 844-847, see especially pages 846-847, Methods.	1-14
Y		15-20
X, P	BUBENDORF et al. Hormone therapy failure in human prostate cancer: analysis by complementary DNA and tissue microarrays. J. Nat. Cancer Inst. 20 October 1999, Vol. 91, No. 20, pages 1758-1764, see especially pages 1759-1760, Materials and Methods.	1-14
Y, P		15-20
X	MOCH et al. High-throughput tissue microarray analysis to evaluate genes uncovered by cDNA microarray screening in renal cell carcinoma. Am. J. Pathol. April 1999, Vol. 154, No. 4, pages 981-986, see especially pages 982-983, Materials and Methods.	1-14
Y		15-20
X	BUBENDORF et al. Survey of gene amplification during prostate cancer progression by high-throughput fluorescence in situ hybridization on tissue microarray. Cancer Res. 15 February 1999, Vol. 59, pages 803-806, see especially pages 803-804, Materials and Methods.	1-14
Y		15-20

☒ Further documents are listed in the continuation of Box C.

☐ See patent family annex.

Special categories of cited documents:	
"A" document defining the general state of the art which is not considered to be of particular relevance	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"E" earlier application or patent published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family
"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

03 November 2000 (03.11.2000)

Date of mailing of the international search report

18 DEC 2000

Name and mailing address of the ISA/US

Commissioner of Patents and Trademarks

Box PCT

Washington, D.C. 20231

Facsimile No. (703)305-3230

Authorized officer

Minh-Quan K. Pham

Telephone No. (703) 308-0196

DELLA MAE COLLINS
PARALEGAL SPECIALIST
TECHNOLOGY CENTER 1600

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US00/26113

C (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X — Y	BUBENDORF et al. High-throughput survey of gene amplification underlying prostate cancer progression using a novel tissue microarray ("tissue chip") technology. J. Urol. 02 May 1999, Vol. 161, No. 4 Suppl., page 51, Number 187, see entire document.	1-14 — 15-20
X — Y	MOCH et al. High-throughput tissue microarray analysis to evaluate prognostic significance of genes uncovered by cDNA microarray screening. J. Urol. 03 May 1999, Vol. 161, No. 4 Suppl., page 140, Number 535, see entire document.	1-14 — 15-20
X — Y	BUBENDORF et al. High-throughput survey of gene amplification underlying prostate cancer progression using a novel tissue microarray ("tissue chip") technology. Proc. Am. Assoc. Cancer Res. March 1999, Vol 40, page 536, Number 3535, see entire document.	1-14 — 15-20
X — Y	KONONEN et al. Tumor tissue microarrays for high-throughput in situ analysis of gene copy number and expression from hundreds of cancer specimens. Proc. Am. Assoc. Cancer Res. March 1998, Vol. 39, pages 454-455, Number 3093, see entire document.	1-14 — 15-20
Y	BATTIFORA, H. The multitumor (sausage) tissue block: novel method for immunohistochemical antibody testing. Lab. Invest. 1986, Vol. 55, No. 2, pages 244-248, see especially pages 244-247, Materials and Methods.	1-20
Y	RICHTER ET AL. "Tissue Chips" to rapidly evaluate the clinical significance of genomic alterations detected by CGH. Cytogenet. Cell Genet. 1999, Vol. 85, No. 1-2, page 129, Number P531, see entire document.	1-20
Y	SAUTER ET AL. Tissue chips for high throughput molecular analysis of tumors. Cytogenet Cell Genet. 1999, Vol. 85, No. 1-2, page 19, Number O 058, see entire document.	1-20